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13. ABSTRACT (*Maximum 200 words*)

The goal of this research is to develop thermodynamically correct bioavailability estimations using chromatographic stationary phases as a model of the "interphase" system. It has been previously established that octanol-water partition coefficients are not thermodynamically relevant for the modeling of bioaccumulation processes (Opperhuizen et al., Environ. Sci. Technol. 1988, 22, 286). They investigated the thermodynamic properties of the partitioning of chlorobenzenes between fish lipids and water, and showed that bioconcentration is accompanied by positive enthalpy and entropy changes. In contrast, the partitioning of these compounds between octanol and water is accompanied by negative enthalpy and by small negative or positive entropy changes. They conclude that the difference in the thermodynamic properties of these processes arise from the different structures of fish lipids and octanol, and that only under very specific conditions and only for structurally similar compounds can a relationship between octanol-water partitioning and bioaccumulation be expected.

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"Thermodynamically Correct Bioavailability Estimations"

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The goal of this research is to develop thermodynamically correct bioavailability estimations using chromatographic stationary phases as a model of the "interphase" system. It has been previously established that octanol-water partition coefficients are not thermodynamically relevant for the modeling of bioaccumulation processes (Opperhuizen et al., *Environ. Sci. Technol.* **1988, 22**, 286). They investigated the thermodynamic properties of the partitioning of chlorobenzenes between fish lipids and water, and showed that bioconcentration is accompanied by *positive* enthalpy and entropy changes. In contrast, the partitioning of these compounds between octanol and water is accompanied by *negative* enthalpy and by small negative or positive entropy changes. They conclude that the differences in the thermodynamic properties of these processes arise from the different structures of fish lipids and octanol, and that only under very specific conditions and only for structurally similar compounds can a relationship between octanol-water partitioning and bioaccumulation be expected.

We have spent the past ten years investigating the molecular mechanism of retention of reversed phase liquid chromatography (RPLC), and have shown that at sufficiently high bonded chain density, partitioning of solutes to reversed phase chromatographic stationary phases match the partitioning thermodynamics between fish lipids and water measured by Opperhuizen.

I will briefly summarize the most significant results of our research, further details can be found in the publications resulting from this work, listed at the end of this report.

First, we spent significant effort to further characterize and understand the partitioning process of small molecules between bulk solutions and our chromatographic stationary phases. We performed EPR experiments, DSC experiments, and thermodynamic measurements, all of which show that the chain ordering of the stationary phase is important to the partitioning process, and that the entropic contribution to retention becomes more significant with respect to the enthalpic contribution as the stationary phase bonding density is increased.

We have also made significant progress toward our goal of using our well characterized stationary phases for modeling bioaccumulation processes. Our most important paper in this area shows results just as we anticipated. We measured chromatographic retention for pesticides, PAH compounds and barbiturates on an RPLC column with high alkyl chain density, and in all cases, correlations of the retention in 100% water mobile phases with bioavailability are equivalent to or better than correlations of bioavailability with the octanol-water partition coefficient.

We have also made significant progress on the use of capillary electrophoresis for the estimation of these processes. While liquid chromatography has been the most studied method of estimating octanol-water partition coefficients and the processes that the octanol-water coefficient is supposed to model, it is a time consuming and labor intensive method. We have just shown that capillary electrophoresis may be able to give a *single point* estimate of the octanol-water partition coefficient, and we are currently investigating ways of modifying the CE experiment to more closely match the thermodynamics shown in the chromatographic process.

In summary, we have met the goals of our original proposal, and these results have been published in the open literature. Following is a list of refereed papers which acknowledge AFOSR support published or accepted during the sponsorship from AFOSR:

1. "Microscopic Order as a Function of Surface Coverage in Alkyl Modified Silicas: Spin Probe Studies", Paul B. Wright, Edward Lamb, John G. Dorsey and Robert G. Kooser, *Anal. Chem., 64,* 785-789 (1992).

2. "Temperature Dependence of Retention in Reversed Phase Liquid Chromatography: Stationary Phase Considerations", Lynn A. Cole and John G. Dorsey, *Anal. Chem., 64,* 1317-1323 (1992).

3. "Temperature Dependence of Retention in Reversed Phase Liquid Chromatography: Mobile Phase Considerations", Lynn A. Cole, John G. Dorsey and Ken A. Dill, *Anal. Chem., 64,* 1324-1327 (1992).

4. "Liquid Chromatography: Theory and Methodology", John G. Dorsey, Joe P. Foley, William T. Cooper, Robert A. Barford and Howard G. Barth, *Anal. Chem., 64,* 353R-389R (1992).

5. "Accurate Determination of log k'_W in Reversed Phase Liquid Chromatography: Implications for Quantitative Structure Retention Relationships", Mei-Ming Hsieh and John G. Dorsey, *J. Chromatogr., 631,* 63-78 (1993).

6. "The Effect of Stationary Phase Solvation on Shape Selectivity in Reversed Phase Liquid Chromatography", Steven R. Cole and John G. Dorsey, *J. Chromatogr., 635,* 177-186 (1993).

7. "Phase Transitions of Reversed Phase Stationary Phases: Cause and Effects in the Mechanism of Retention", John F. Wheeler, Thomas L. Beck, S. J. Klatte, Lynn A. Cole and John G. Dorsey, *J. Chromatogr., 656,* 317–333 (1993).

8. "Hydrophobicity Estimations by Reversed Phase Liquid Chromatography: Implications for Biological Partitioning Processes", John G. Dorsey and Morteza G. Khaledi, *J. Chromatogr., 656,* 485–499 (1993).

9. "Retention Mechanisms of Bonded Phase Liquid Chromatography", John G. Dorsey and William T. Cooper, *Anal. Chem.*, *66*, 857A-867A (1994).

10. "Liquid Chromatography: Theory and Methodology", John G. Dorsey, Joe P. Foley, William T. Cooper, John F. Wheeler and Howard G. Barth, *Anal. Chem.*, *66*, 500R-546R (1994).

11. "Bioavailability Estimation by Reversed-Phase Liquid Chromatography: High Bonding Density C-18 Phases for Modeling Biopartitioning Processes", Mei-Ming Hsieh and John G. Dorsey, *Anal. Chem.*, *67*, 48-57 (1995).

12. "n-Octanol-Water Partition Coefficient Estimation by Micellar Electrokinetic Capillary Chromatography", Bradford J. Herbert and John G. Dorsey, *Anal. Chem.*, *67*, 744-749 (1995).

13. "Silver (I) Mediated Separations by Capillary Zone Electrophoresis and Micellar Electrokinetic Chromatography: Argentation Electrophoresis", Paul B. Wright and John G. Dorsey, *Anal. Chem.*, *68*, 415-424 (1996).

14. "The Informational Orthogonality of 2-Dimensional Chromatographic Separations", Patrick J. Slonecker, Xiaodong Li, Thomas H. Ridgway and John G. Dorsey, *Anal. Chem.*, *68*, 682-689 (1996).